

Remarks

Reconsideration of the above identified application in view of the preceding amendments and following remarks is respectfully requested. Claims 1-8 and 13-26 will be pending upon entry of this paper. By this Amendment, Applicants have amended Claim 8 and added Claims 25 and 26. These amendments have not been necessitated by the need to distinguish the present invention from any prior art and were made solely to more fully claim the invention. It is respectfully submitted that no new matter has been introduced by these amendments, as support therefor is found throughout the specification and drawings.

Claim Objections

In the Office Action, Claim 8 was objected to as having a typographical error. Claim 8 has been corrected and an action acknowledging the same is respectfully requested.

35 U.S.C. §102

In the Office Action, Claims 1-5, 7 and 8 were rejected under 35 U.S.C. §102(b) as being anticipated by Clark et al. (the Clark reference).

The Clark reference discloses cell guidance by ultrafine topography of grating surfaces. Once the fused quartz is patterned, the grating surfaces have a single type of cell guided thereon such as chick embryo cerebral neurones.

In contrast, Claim 1 recites a substrate having micromachined surface structures provided thereon, wherein said micromachined surface structures comprise nanotopographic features superimposed thereon, the nanotopographic features being arranged in such a manner so as to organize multiple cell types into desired

subassemblies within said micromachined surface structures. Consequently, multiple cell types are organized into subassemblies. The Clark reference does not disclose such a structure because it is simply limited to a discussion of how individual cell types respond. Accordingly, Claim 1 and each of the remaining claims depending therefrom distinguish the subject invention from the Clark reference. Therefore, withdrawal of the rejection is respectfully requested.

In the Office Action, Claims 1-8, 13, 15, 17 and 19-24 were rejected under 35 U.S.C. §102(a) as being anticipated by Desai 2000 (the Desai reference).

The Desai reference discloses nanotechnology to recreate complex tissue architecture. The tissue-engineered replacement is a scaffold in which a given cell population is seeded. Similar to the Clark reference, the Desai reference does not disclose using nanotopographic features to organize multiple cell types into subassemblies.

As noted above, Claim 1 recites, *inter alia*, the nanotopographic features being arranged in such a manner so as to organize multiple cell types into desired subassemblies within said micromachined surface structures. The Desai reference does not disclose such a structure. Accordingly, Claim 1 and each of the remaining claims depending therefrom distinguish the subject invention from the Desai reference and an action acknowledging the same is respectfully requested.

Turning to Claim 13, it recites a tissue engineered system comprising one or more layers, wherein each layer includes micromachined surface structures having nanotopographic features superimposed thereon, the nanotopographic features being

arranged in such a manner so as to organize multiple cell types into desired subassemblies within said micromachined surface structures. The Desai reference does not disclose such a structure of nanotopographic features being arranged in such a manner so as to organize multiple cell types into desired subassemblies. Accordingly, Claim 13 and each of the remaining claims depending therefrom distinguish the subject invention from the Desai reference and an action acknowledging the same is respectfully requested.

35 U.S.C. §103

In the Office Action, Claims 1-8 and 13-24 were rejected under 35 U.S.C. §103(a) as being unpatentable over the Desai reference in view of Borenstein et al. (the Borenstein reference) and U.S. Patent No. 5,665,596 (the '596 patent).

As noted above, the Desai reference discloses nanotechnology to recreate complex tissue architecture. The tissue-engineered replacement is a scaffold in which a given cell population is seeded.

The Borenstein reference discloses micromachining and polymer replica molding towards the field of tissue engineering and notes the requirement for a vascular supply for nutrient and metabolite transport.

The '596 patent discloses cell co-culturing on both sides of a porous membrane. The '596 patent does not comprehend channels, and therefore it does not follow that the '596 patent could ever obviate a centrally positioned membrane whose sole purpose is to enable fluid but not large solute/cell transport across a centrally positioned membrane dividing microchannels. The Desai reference is also silent on this.

It is respectfully submitted that the additional two references do not overcome the deficiencies of the Desai reference, as noted above with respect to Claim 13. In particular, the Borenstein reference and '596 patent do not disclose using nanotopographic features to organize multiple cell types into subassemblies, which is also similar to a limitation of Claim 1. Accordingly, Claims 1, 13 and each of the claims depending therefrom are not rendered obvious by the combination of references cited by the Examiner and withdrawal of the rejection under 35 U.S.C. §103 (a) is respectfully requested.

For completeness, it is also respectfully submitted that one skilled in the art to which the subject invention appertains would not have been motivated to make the three-way combination of the Desai reference, the Borenstein reference and the '596 patent as suggested by the Examiner. The '596 patent simply relates to cell co-culturing and, thus, one would not look to employ it in tissue engineering.

Further, the resulting combination is non-sensical. The '596 patent basically teaches a transwell device, and if you combine it with the Desai reference, the result is a transwell dividing a microfluidic chamber. There is no connection between that resulting structure and a microvascular network or bifurcated microchannel network divided by a centrally positioned membrane say, for example, as recited in Claim 16. Thus, the combination is not proper and withdrawal of the rejection under 35 U.S.C. §103 (a) is respectfully requested.

Furthermore, even if the references were combined as suggested by the Examiner, at best, the Desai reference, the Borenstein reference and the '596 patent result in a

transwell membrane dividing two microfluidic compartments containing cells, perhaps with nanotopography superimposed to influence the cell behavior on one or both sides. The invention of Claim 16 patentably distinguishes over such a structure of having, *inter alia*, a tissue engineered system including each layer having micromachined surface structures having nanotopographic features superimposed thereon, the nanotopographic features being arranged in such a manner so as to organize multiple cell types into desired subassemblies within said micromachined surface structures, wherein channels are divided longitudinally into two compartments by a centrally positioned membrane, and wherein each compartment comprises a different cell type. The claimed invention is far more biomimetic, complex and powerful than the hypothetical combination the Examiner is invoking.

Claim 18 recites, *inter alia*, nutrient supply and excretion removal lines in fluid communication with the system. Again, the three-way combination is only possible by using the teachings of this application to arrive at such a structure, which is impermissible hindsight reconstruction. In view of the above, Claims 16 and 18 have additional structural features that patentably distinguish of the cited combination and an action acknowledging the same is respectfully requested.

Double Patenting

In the Office Action, various claims were rejected under the judicially created doctrine of double patenting. In order to overcome the non-statutory double patenting rejection, Applicants submit herewith terminal disclaimers that should obviate the

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rejection under the judicially created doctrine of double patenting and an action acknowledging same is respectfully requested.

New Claims

Applicant has added new Claims 25 and 26 which are directed to additional patentable aspects of the subject invention. Applicant respectfully submits that new Claims 25 and 26 patentably distinguish over the art of record, and allowance of this claim is respectfully requested.

Any additional fees or overpayments due as a result of filing the present paper may be applied to Deposit Account No. 04-1105. It is respectfully submitted that all of the claims now remaining in this application are in condition for allowance, and such action is earnestly solicited.

If after reviewing this amendment, the Examiner believes that a telephone interview would facilitate the resolution of any remaining matters the undersigned attorney may be contacted at the number set forth herein below.

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Customer No.: 21874

Respectfully submitted,

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